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NEWS 8 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/  
USPAT2  
NEWS 9 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB  
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NEWS 15 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist  
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NEWS 17 FEB 22 The IPC thesaurus added to additional patent databases on STN  
NEWS 18 FEB 22 Updates in EPFULL; IPC 8 enhancements added  
  
NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,  
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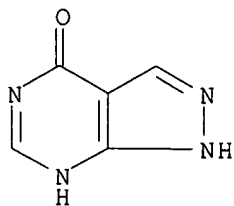
<http://www.cas.org/ONLINE/UG/regprops.html>

=> s allopurinol  
L1 24 ALLOPURINOL

=> s allopurinol/cn  
L2 1 ALLOPURINOL/CN

=> d str rn cn

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

RN 315-30-0 REGISTRY  
 CN 4H-Pyrazolo[3,4-d]pyrimidin-4-one, 1,5-dihydro- (7CI, 8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1,5-Dihydro-1H-pyrazolo[3,4-d]pyrimidin-4-one  
 CN 1H-Pyrazolo[3,4-d]pyrimidin-4-ol  
 CN 4-Hydroxy-1H-pyrazolo[3,4-d]pyrimidine  
 CN 4-Hydroxypyrazolo[3,4-d]pyrimidine  
 CN 4-Oxopyrazolo[3,4-d]pyrimidine  
 CN Adenock  
 CN Allopur  
 CN **Allopurinol**  
 CN Allopurinol(I)  
 CN Allozym  
 CN Allurtal  
 CN Aloral  
 CN Alositol  
 CN Anoprolin  
 CN Anzief  
 CN Apulonga  
 CN Apurin  
 CN Apurol  
 CN Atisuril  
 CN Bleminol  
 CN Bloxanth  
 CN BW 15658  
 CN BW 56-158  
 CN Caplenal  
 CN Cellidrin  
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 CN Embarin  
 CN Epidropal  
 CN Foligan  
 CN Geapur  
 CN Gichtex  
 CN Gotax  
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 CN Ledopur  
 CN Lopurin  
 CN Lysuron  
 CN Milurit  
 CN Miniplanor  
 CN Monarch  
 CN Nektrohan  
 CN NSC 101655  
 CN NSC 1390  
 CN Remid  
 CN Riball  
 CN Sigapuro1

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 COST IN U.S. DOLLARS  
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SINCE FILE	TOTAL
ENTRY	SESSION
12.30	12.51

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=> s 315-30-0/rn

2339 315-30-0

41 315-30-0D

L3 2312 315-30-0/RN

(315-30-0 (NOTL) 315-30-0D )

=> e hypertension

E1 2 HYPERTENSIO/BI

E2 3 HYPERTENSIogenic/BI

E3 76753 --> HYPERTENSION/BI

E4 1 HYPERTENSION1/BI

E5 1 HYPERTENSION3/BI

E6 2 HYPERTENSION5/BI

E7 3 HYPERTENSIONAL/BI

E8 1 HYPERTENSIONC/BI

E9 1 HYPERTENSIOND/BI

E10 1 HYPERTENSIONGENIC/BI

E11 1 HYPERTENSIONN/BI

E12 1 HYPERTENSIONOGENIC/BI

=> s e3

76753 HYPERTENSION/BI

97 HYPERTENSIONS/BI

L4 76773 HYPERTENSION/BI

((HYPERTENSION OR HYPERTENSIONS)/BI)

=> s L3 and L4

L5 43 L3 AND L4

=> s L5 and (AY<2001 or PY<2001 or PRY<2001)

3387339 AY<2001

20847148 PY<2001

3325017 PRY<2001

L6 23 L5 AND (AY<2001 OR PY<2001 OR PRY<2001)

=> dup rem L6

PROCESSING COMPLETED FOR L6

L7 23 DUP REM L6 (0 DUPLICATES REMOVED)

=> s L5 and (AY<2000 or PY<2000 or PRY<2000)  
3148993 AY<2000  
19940782 PY<2000  
3080746 PRY<2000  
L8 20 L5 AND (AY<2000 OR PY<2000 OR PRY<2000)

=> d 1-23 L7 ibib abs

L7 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2002:10270 CAPLUS  
DOCUMENT NUMBER: 136:64126  
TITLE: Agent reducing uric acid levels for treatment of  
cardiovascular disease and **hypertension**  
INVENTOR(S): Kivlighn, Salah; Johnson, Richard J.; Mazzali, Marilda  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; University of Washington  
SOURCE: PCT Int. Appl., 49 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000210	A2	20020103	WO 2001-US20457	20010628 <--
WO 2002000210	A3	20021024		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413201	AA	20020103	CA 2001-2413201	20010628 <--
AU 2001068734	A5	20020108	AU 2001-68734	20010628 <--
US 2002019360	A1	20020214	US 2001-892505	20010628 <--
EP 1317258	A2	20030611	EP 2001-946722	20010628 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517804	T2	20040617	JP 2002-504992	20010628 <--
PRIORITY APPLN. INFO.: US 2000-214825P P 20000628 <-- WO 2001-US20457 W 20010628				

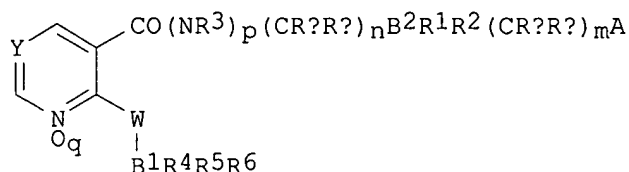
AB This invention relates to a method for treating and preventing **hypertension** by administering a therapeutically effective amount of an agent capable of reducing uric acid levels in a patient in need of such treatment. Addnl., the scope of the invention includes a method of treating coronary heart disease by administering a therapeutically effective amount of an agent capable of reducing uric acid levels in a patient in need of such treatment. Allopurinol administered from the initiation of an oxonic acid diet prevented the development of hyperuricemia and **hypertension**. In hypertensive, hyperuricemic rats, either withdrawal of the oxonic acid or adding allopurinol also resulted in a reduction in the blood pressure in association with a fall in serum uric acid values.

L7 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2002:591707 CAPLUS  
DOCUMENT NUMBER: 137:140509  
TITLE: Preparation of nicotinamides and mimetics as  
inhibitors of phosphodiesterase IV isozymes  
INVENTOR(S): Chambers, Robert J.; Magee, Thomas V.; Marfat, Anthony

PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: Eur. Pat. Appl., 180 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1229034	A1	20020807	EP 2002-250202	20020111
EP 1229034	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 293109	E	20050415	AT 2002-250202	20020111
ES 2239203	T3	20050916	ES 2002-2250202	20020111
CA 2369462	AA	20020731	CA 2002-2369462	20020129
US 2002111495	A1	20020815	US 2002-62811	20020131 <--
BR 2002000250	A	20021008	BR 2002-250	20020131
US 2004171798	A1	20040902	US 2004-781062	20040217
PRIORITY APPLN. INFO.:			US 2001-265240P	P 20010131
			US 1997-43403P	P 19970404 <--
			US 1998-105120P	P 19981021 <--
			US 2002-62811	B1 20020131

OTHER SOURCE(S): MARPAT 137:140509  
 GI



AB Title compds. [I; p, q = 0, 1; m = 0-2; n = 1, 2; A = CO2R7, CONR9CO2R7, CONR7R9, OP(O)(OH)2, SO3H, acylsulfonamido, etc.; W = O, S, SO, SO2, NR3; Y = N, NO, CR11; R1, R2 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, etc.; R3 = H, alkyl, Ph, PhCH2, etc.; R4-R6 = H, F, Cl, alkynyl, cyano, NO2, etc.; R7 = H, (substituted) alkyl, alkenyl, alkynyl; R9 = H, alkyl, cycloalkyl, Ph, PhCH2, pyridyl, etc.; R11 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, fluoroalkoxy, etc.; Ra, Rb = H, F, CF3, alkyl, (substituted) cycloalkyl, Ph, PhCH2; B1, B2 = 3-7 membered (hetero)cyclyl, 7-12 membered poly(hetero)cyclyl; pairs of variables may form rings; with provisos], were prepared (no data). Thus, Me 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionate was suspended in Me3COH. Aqueous NaOH was added to the suspension, and the reaction mixture was refluxed 1 h to give 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionic acid.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103 <--
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105 <--  
US 2000-196571P P 20000411 <--

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L7 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:861482 CAPLUS

DOCUMENT NUMBER: 134:32977

TITLE: Methods and compositions for the treatment of neuroleptic and related disorders using sertindole derivatives

INVENTOR(S): Jerussi, Thomas P.

PATENT ASSIGNEE(S): Sepracor Inc., USA

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072837	A2	20001207	WO 2000-US14984	20000531 <--
WO 2000072837	A3	20010517		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,

AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6489341 B1 20021203 US 2000-580492 20000530 <--  
PRIORITY APPLN. INFO.: US 1999-137447P P 19990602 <--  
US 2000-580492 A 20000530 <--

AB The invention relates to novel methods using, and pharmaceutical compns.  
and dosage forms comprising, sertindole derivs. Sertindole derivs.  
include, but are not limited to, nor-sertindole, 5-oxo-sertindole,  
dehydro-sertindole, and dehydro-nor-sertindole. The methods of the  
invention are directed to the treatment and prevention of neuroleptic and  
related disorders such as, but are not limited to, psychotic disorders,  
depression, anxiety, substance addiction, memory impairment and pain. For  
example, capsules were prepared containing a sertindole derivative 50.0 mg,  
lactose  
48.5 mg, TiO<sub>2</sub> 0.5 mg, and Mg stearate 1.0 mg.

L7 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:259979 CAPLUS

DOCUMENT NUMBER: 132:288794

TITLE: Sympathetic nervous system activity-reducing agents  
for treatment of disease- or age-related weight loss  
and for enhancement of exercise performance

INVENTOR(S): Anker, Stefan Dietmar; Coats, Andrew Justin Stewart

PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021509	A2	20000420	WO 1999-GB3302	19991015 <--
WO 2000021509	A3	20001109		
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1121111	A2	20010808	EP 1999-947762	19991015 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002527378	T2	20020827	JP 2000-575485	19991015 <--
PRIORITY APPLN. INFO.:			GB 1998-22458	A 19981015 <--
			GB 1998-22459	A 19981015 <--
			GB 1999-17181	A 19990723 <--
			WO 1999-GB3302	W 19991015 <--

AB A method of treating weight loss due to underlying disease in a patient, the  
method comprising administering to the patient an effective amount of an  
agent which reduces sympathetic nervous system activity. A method of  
treating weight loss due to underlying disease in a patient, the method  
comprising administering to the patient an effective amount of any one or  
more of the following: a compound which inhibits the effect of aldosterone  
such as an aldosterone antagonist; a chymase inhibitor; a cathepsin B  
inhibitor; a  $\beta$  receptor blocker; an imidazoline receptor antagonist;  
a centrally acting  $\alpha$  receptor antagonist; a peripherally acting  
 $\alpha$  receptor antagonist; a ganglion blocking agent; a drug that has an  
effect on cardiovascular reflexes and thereby reduces SNS activity such as  
an opiate; scopolamine; an endothelin receptor antagonist; and a xanthine  
oxidase inhibitor. The methods are particularly useful in treating  
cardiac cachexia. The sympathetic nervous system activity-reducing agents  
may also be used to treat weight loss due to aging and to enhance exercise  
performance.



L7 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:229952 CAPLUS

DOCUMENT NUMBER: 132:260495

TITLE: Allopurinol normalizes endothelial dysfunction in type 2 diabetics with mild **hypertension**

AUTHOR(S): Butler, Robert; Morris, Andrew D.; Belch, Jill J. F.; Hill, Alexander; Struthers, Allan D.

CORPORATE SOURCE: University Department of Clinical Pharmacology and Therapeutics, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK

SOURCE: Hypertension (2000), 35(3), 746-751

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Therapeutic strategies against free radicals have mostly focused on the augmentation of antioxidant defenses (eg, vitamins C and E). A novel approach is to prevent free radical generation by the enzyme system xanthine oxidase. We examined whether the inhibition of xanthine oxidase with allopurinol can improve endothelial function in subjects with type 2 diabetes and coexisting mild **hypertension** compared with control subjects of a similar age. We examined 23 subjects (11 patients with type 2 diabetes and 12 healthy age-matched control subjects) in 2 parallel groups. The subjects were administered 300 mg allopurinol in a randomized, placebo-controlled study in which both therapies were administered for 1 mo. Endothelial function was assessed with bilateral venous occlusion plethysmog., in which the forearm blood flow responses to intra-arterial infusions of endothelium-dependent and -independent vasodilators were measured. Allopurinol significantly increased the mean forearm blood flow response to acetylcholine by 30% ( $3.16 \pm 1.21$  vs.  $2.54 \pm 0.76$  mL  $\cdot$  100 mL $^{-1}$   $\cdot$  min $^{-1}$  allopurinol vs. placebo;  $P=0.012$ , 95% CI 0.14, 1.30) but did not affect the nitroprusside response in patients with type 2 diabetes. There was no significant impact on either endothelium-dependent or -independent vascular responses in age-matched control subjects. Allopurinol improved endothelial function to near-normal levels. Regarding markers of free radical activity, the level of malondialdehyde was significantly reduced ( $0.30 \pm 0.04$  vs.  $0.34 \pm 0.05$   $\mu$ mol/L for allopurinol vs. placebo,  $P=0.03$ ) in patients with type 2 diabetes but not in control subjects. The xanthine oxidase inhibitor allopurinol improves endothelial dysfunction in patients with type 2 diabetes with mild **hypertension** but not in matched control subjects. In the former group, allopurinol restored endothelial function to near-normal levels.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:327858 CAPLUS

DOCUMENT NUMBER: 135:205240

TITLE: Effect of losartan and furosemide on the urinary excretion of oxypurinol and uric acid

AUTHOR(S): Yamamoto, Tetsuya; Moriwaki, Yuji; Takahashi, Sumio; Tsutsumi, Zenta; Hada, Toshikazu

CORPORATE SOURCE: Third Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan

SOURCE: Advances in Experimental Medicine and Biology (2000), 486(Purine and Pyrimidine Metabolism in Man X), 185-188

CODEN: AEMBAP; ISSN: 0065-2598

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Losartan potassium (losartan) is an angiotensin II receptor antagonist

used for the treatment of **hypertension**, which opposes the action of angiotensin II at the AT1 receptor. On the other hand, furosemide is a diuretic and is used for the treatment of heart failure, **hypertension** and edema. A study was conducted to determine whether losartan and furosemide affect the urinary excretion of the allopurinol metabolite oxypurinol together with uric acid. The urinary excretion of uric acid increased by 4.1-fold, and that of oxypurinol by 2-fold, from 1 to 2 h after the administration of losartan. In addition, the fractional clearance of uric acid increased by 4.3-fold, and that of oxypurinol by 2.2-fold from 1 to 2 h after the administration of losartan potassium. Meanwhile, the urinary excretion of uric acid decreased by 43%, and that of oxypurinol by 40%, from 1 to 2 h after the administration of furosemide. Also, the fractional clearance of uric acid decreased by 46% and that of oxypurinol by 39%, from 1 to 2 h after the administration of furosemide. The plasma concentration of total protein increased by 9% at 1.5 h after administration of furosemide. In the control study, these values did not change.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:231552 CAPLUS

DOCUMENT NUMBER: 130:249107

TITLE: System and method for measuring hydrogen peroxide levels in a fluid and method for assessing oxidative stress

INVENTOR(S): Lacy, Fred; Schmid-Schonbein, Geert W.; Gough, David

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9915891	A1	19990401	WO 1998-US19013	19980914 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9894805	A1	19990412	AU 1998-94805	19980914 <--
PRIORITY APPLN. INFO.:			US 1997-60010P	P 19970925 <--
			WO 1998-US19013	W 19980914 <--

AB The detection system includes a pair of electrochem. hydrogen peroxide sensors, each sensor having working, counter and reference electrodes. A bias voltage is applied to maintain a voltage difference between the working and reference electrodes. A sample aliquot of fluid was treated with either sodium azide or catalase. The sensors are placed in containers containing sufficient amts. of treated fluid to cover the active portions of the electrodes. The output current of each sensor is amplified, and the resulting amplified signals are combined and subtracted to provide a signal which is representative of the level of hydrogen peroxide in the fluid. In a method for assessing oxidative stress, including that related to essential **hypertension**, the detection system is used to determine a representative level of hydrogen peroxide in blood plasma drawn from a test subject. The level of hydrogen peroxide is directly related to the level of reactive oxygen species in the plasma, and can be used as an accurate predictor of risk for essential **hypertension** or other

conditions related to oxidative stress. Blood plasma samples of normotensive subjects and patients with essential **hypertension** were analyzed by the system. When hypertensives were compared with family history neg. normotensives, it was found that the hypertensive group had a higher mean arterial pressure by 23% as well as higher levels of plasma hydrogen peroxide by 48% over the normotensive control.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:717166 CAPLUS

DOCUMENT NUMBER: 132:192650

TITLE: Pathogenic role of oxidative stress in vascular angiotensin-converting enzyme activation in long-term blockade of nitric oxide synthesis in rats

AUTHOR(S): Usui, Makoto; Egashira, Kensuke; Kitamoto, Shiro; Koyanagi, Masamichi; Katoh, Makoto; Kataoka, Chu; Shimokawa, Hiroaki; Takeshita, Akira

CORPORATE SOURCE: Research Institute of Angiocardiology and Cardiovascular Clinic, Kyushu University Faculty of Medicine, Fukuoka, 812-8582, Japan

SOURCE: Hypertension (1999), 34(4, Pt. 1), 546-551  
CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibition of nitric oxide (NO) synthesis with N $\omega$ -nitro-L-arginine Me ester (L-NAME) activates vascular angiotensin-converting enzyme (ACE) and causes oxidative stress. We investigated the role of oxidative stress in the pathogenesis of ACE activation in rats. Studies involved aortas of rats receiving no treatment, L-NAME, L-NAME plus L-arginine, or L-NAME plus an antioxidant drug (N-acetylcysteine, allopurinol, or ebselen) for 7 days. L-NAME significantly increased oxidative stress (O $_2$ -) and ACE activity. The increased O $_2$ - production was normalized by removal of endothelium. Immunohistochem. showed the increased ACE activity in the endothelial layer. Treatment with antioxidant drugs did not affect the L-NAME-induced increase in systolic arterial pressure but did prevent increases in vascular O $_2$ - production and ACE activity. These results implicate oxidative stress in the pathogenesis of vascular ACE activation in rats with long-term inhibition of NO synthesis. The observed effects of antioxidant drugs on ACE activation do not appear to involve the **hypertension** induced by L-NAME.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:56067 CAPLUS

DOCUMENT NUMBER: 130:218034

TITLE: Exposure to allopurinol and the risk of cataract extraction in elderly patients

AUTHOR(S): Garbe, Edeltraut; Suissa, Samy; LeLorier, Jacques

CORPORATE SOURCE: Potsdam Institute of Pharmacoepidemiology, Technology Assessment, Potsdam, Germany

SOURCE: Archives of Ophthalmology (Chicago) (1998), 116(12), 1652-1656

CODEN: AROPAW; ISSN: 0003-9950

PUBLISHER: American Medical Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objective: To determine whether exposure to allopurinol is associated with an increased risk of cataract extraction in elderly patients. Methods: We conducted a case-control study using data from the Quebec universal health insurance program for all elderly patients. The 3677 cases were patients with a cataract extraction between 1992 and 1994. The 21 868 controls were

randomly selected among patients not diagnosed with cataract and matched to cases on the date of the extraction. We determined the odds ratio of cataract extraction according to the cumulative dose and duration of allopurinol use relative to nonusers, using conditional logistic regression anal. The anal. was adjusted for the effects of age, sex, diabetes mellitus, **hypertension**, glaucoma, and ophthalmic and oral corticosteroid exposure. Results: A cumulative dose of allopurinol of more than 400 g or a duration of use of longer than 3 yr were associated with an increased risk of cataract extraction, with odds ratios of 1.82 (95% confidence interval [CI], 1.18-2.80) and 1.53 (95% CI, 1.12-2.08), resp. No increase in risk was observed for lower cumulative doses or shorter exposure periods. Conclusion: Long-term administration of allopurinol increases the risk of cataract extraction in elderly patients.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:671552 CAPLUS

DOCUMENT NUMBER: 130:34174

TITLE: Role of xanthine oxidase in hydrogen peroxide production

AUTHOR(S): Lacy, Fred; Gough, David A.; Schmid-Schonbein, Geert W.

CORPORATE SOURCE: Department of Bioengineering, Institute for Biomedical Engineering, University of California at San Diego, La Jolla, CA, 92093-0412, USA

SOURCE: Free Radical Biology & Medicine (1998), 25(6), 720-727

CODEN: FRBMEH; ISSN: 0891-5849

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Increased production of oxygen free radicals may play a role in many diseases such as **hypertension**. As evidence indicates that xanthine oxidase may be involved in creating these reactive oxygen species, expts. were performed to addnl. characterize hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) production in xanthine oxidase-catalyzed reactions. In vitro measurements of hydrogen peroxide production from the xanthine/xanthine oxidase reaction were performed in buffered saline using an electrochem. technique, and the effect of allopurinol on inhibition of xanthine oxidase was determined. Expts. were also performed in blood plasma to characterize endogenous hydrogen peroxide-producing capability and xanthine oxidase activity. In the presence of sodium azide, an inhibitor of catalase, peroxide production was measured in plasma after adding xanthine or xanthine oxidase and the results were similar to those obtained in buffered saline. When only sodium azide was added to plasma, hydrogen peroxide was produced at a level of  $36.1 \pm 7.6 \mu\text{M}$  (n = 5). From these measurements, endogenous xanthine oxidase activity was estimated to be  $6.5 \pm 0.3 \text{ mU/mL}$  (n = 5). These results suggest that sufficient substrate exists in plasma to produce micromolar levels of hydrogen peroxide and xanthine oxidase may catalyze these reactions.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:569276 CAPLUS

DOCUMENT NUMBER: 129:310723

TITLE: Efficacy of allopurinol in ameliorating the progressive renal disease in familial juvenile hyperuricemic nephropathy (FJHN). A six-year update

AUTHOR(S): McBride, M. B.; Simmonds, H. A.; Ogg, C. S.; Cameron, J. S.; Rigden, S.; Rees, L.; Hoff, W. Van't; Moro, F.; Raman, G. V.

CORPORATE SOURCE: Purine Research, Renal and Paediatric Renal Units,  
UMDS, Guy's Hospital, UK  
SOURCE: Advances in Experimental Medicine and Biology (  
1998), 431(Purine and Pyrimidine Metabolism in  
Man IX, 1998), 7-11  
CODEN: AEMBAP; ISSN: 0065-2598  
PUBLISHER: Plenum Publishing Corp.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Earlier work by the authors showed beneficial effects of allopurinol in 10  
patients with familial juvenile hyperuricemic nephropathy (FJHN) followed  
for up to 23 yr. However, these findings have been disputed by others who  
reported no such effect. Results are now presented of the follow-up of  
many more patients, including siblings recognized as having FJHN during  
biochem. screening. Results confirmed that allopurinol ameliorated the  
rapid decline in renal function seen both previously and in this study in  
75% of subjects. A creatine level of > 200 µmol/l at diagnosis  
indicated poor prognosis. Efficacy of allopurinol depends on good  
compliance, and aggressive control of **hypertension**, if present,  
was also vital.  
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:51850 CAPLUS  
DOCUMENT NUMBER: 128:113673  
TITLE: Possibility of gout complications caused by xanthine  
oxidase and active oxygen  
AUTHOR(S): Matsumoto, Mihuji; Sakano, Shougo  
CORPORATE SOURCE: Dep. Blood Transfus., Nagoya City Univ., Nagoya, 467,  
Japan  
SOURCE: Purin, Pirimijin Taisha (1997), 21(2),  
171-173  
CODEN: PPTAEV; ISSN: 0916-2836  
PUBLISHER: Nippon Purin, Pirimijin Taisha Gakkai  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese

AB Oxidation and denaturing of blood lipids as well as atherosclerotic changes  
were detected in gout patients, and atherosclerosis is a factor selecting  
uric acid controlling medicine in gout. The patients with  
**hypertension**, glucose tolerance anomaly and splanchnic adiposis,  
being atherosclerotic factors, exhibited high lipid peroxide (LPO)  
concentration  
in blood before drug treatment. LPO concentration decreased after treatment in  
patients with decrease in atherosclerotic factors. The concentration was lower  
in patients receiving allopurinol (AP) than benzbromarone (BB). The pos.  
ratio of anti-oxidized and denatured low d. lipoprotein (LDL) antibody was  
higher in BB-treated patients than AP-treated patients in cases with  
administration period >1 yr. In BB-treated patients, the LPO concentration  
increased when hyperuricemia was poorly controlled.

L7 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:565344 CAPLUS  
DOCUMENT NUMBER: 125:244617  
TITLE: Allopurinol reduces bacterial translocation,  
intestinal mucosal lipid peroxidation, and  
neutrophil-derived myeloperoxidase activity in chronic  
portal hypertensive and common bile duct-ligated  
growing rats  
AUTHOR(S): Schimpl, Gunther; Pesendorfer, Patricia; Steinwender,  
Gerhard; Feierl, Gerhard; Ratschek, Manfred;  
Hollwarth, Michael E.  
CORPORATE SOURCE: Medical School, University Graz, A-8036, Austria  
SOURCE: Pediatric Research (1996), 40(3), 422-428

CODEN: PEREBL; ISSN: 0031-3998

PUBLISHER: Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Bacterial translocation (BT) from the gastrointestinal tract has been thought to play a role in the pathogenesis of septic complications in patients with chronic portal **hypertension** (PH) and obstructive jaundice. The purpose of this study was to investigate the incidence of BT and to assess the role of intestinal mucosal malondialdehyde (MDA) levels as an indicator of lipid peroxidn. and polymorphonuclear neutrophil-derived myeloperoxidase (MPO) in chronic portal hypertensive and common bile duct-ligated rats. Twenty male rats were subjected to sham laparotomy (SL), 20 rats to calibrated portal vein constriction (PH), 20 rats to common bile duct ligation (CBDL), and 10 rats served as a nonoperated control group (NOP). After 4 wk, 10 animals of each operated group received 50 mg/kg allopurinol i.p., at 24 h, and again 2 h prior to estimation of BT, intestinal mucosal MDA, and MPO activities. In the NOP and SL groups, BT to the mesenteric lymph nodes (MLN) and spleen was present. In PH and in CBDL rats, BT to liver, portal vein, peritoneum, and caval vein occurred. Allopurinol treatment attenuated the frequency of BT in PH and decreased BT in CBDL rats significantly ( $p < 0.05$ ). Ileal mucosal MDA levels (nanomoles/g) in untreated rats increased from  $45.1 \pm 7.9$  in SL to  $98.2 \pm 9.1$  in PH and to  $102.2 \pm 11$  in CBDL rats ( $p < 0.01$ ). In the allopurinol groups the increase of MDA to  $49.1 \pm 1.3$  in PH, and  $66.2 \pm 2.2$  in CBDL was significantly lower ( $p < 0.01$ ). MPO activity (units/g) in the ileal mucosa increased in untreated rats from  $319 \pm 129$  after SL to  $866 \pm 104$  after PH and to  $1016 \pm 104$  after CBDL ( $p < 0.01$ ). Allopurinol significantly attenuated MPO activity to  $369 \pm 44$  in PH, and to  $372 \pm 60$  in CBDL animals ( $p < 0.01$ ). In PH and CBDL rats significant BT, intestinal mucosal lipid peroxidn., and polymorphonuclear neutrophil-derived MPO activity occurred. Allopurinol reduced BT and improved intestinal mucosal MDA and MPO activities, suggesting that there might be an association between BT and intestinal mucosal lipid peroxidn.

L7 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:207673 CAPLUS  
DOCUMENT NUMBER: 124:313438  
TITLE: Potentiation of nitric oxide-mediated vasorelaxation by xanthine oxidase inhibitors  
AUTHOR(S): Miyamoto, Yoichi; Akaike, Takaaki; Yoshida, Masaki; Goto, Shingo; Horie, Hidechika; Maeda, Hiroshi  
CORPORATE SOURCE: School Medicine, Kumamoto Univ., Kumamoto, 860, Japan  
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1996), 211(4), 366-73  
CODEN: PSEBAA; ISSN: 0037-9727

PUBLISHER: Blackwell  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Nitric oxide (NO), now almost synonymous with endothelium-derived relaxing factor (EDRF), reacts with superoxide anion radical ( $O_2^-$ ) and forms a potentially toxic mol. species, peroxynitrite ( $ONOO^-$ ). Because xanthine oxidase (XO) seems to be a major  $O_2^-$ -producing enzyme in the vascular system, it is important to clarify the mechanism of XO regulation of NO/EDRF. We first characterized the inhibition of XO in vitro by three types of pyrazolopyrimidine derivs. Kinetic studies indicated that 4-amino-6-hydroxypyrazolo[3,4-d]pyrimidine (AHPP) and allopurinol competitively inhibited the conversion of xanthine to uric acid catalyzed by XO, with apparent  $K_i$  values of  $0.17 \pm 0.02$  and  $0.50 \pm 0.03 \mu M$ , resp.; alloxanthine inhibited this conversion in a noncompetitive manner with an apparent  $K_i$  value of  $3.54 \pm 1.12 \mu M$ .  $O_2^-$  generation in the xanthine/XO system assayed by lucigenin-dependent chemiluminescence was suppressed most strongly by AHPP in a dose-dependent fashion; allopurinol itself appears to reduce the enzyme by transfer of an electron to  $O_2$ , thus generating  $O_2^-$ . AHPP significantly augmented EDRF-mediated relaxation of

aortic rings from both rabbits and spontaneously hypertensive rats (SHR) in a dose-dependent manner, whereas allopurinol did not affect the relaxation and only marginal potentiation of the vasorelaxation was observed with alloxanthine. Finally, i.v. injection of AHPP (50.4 mg/kg; 100  $\mu$ mol/300 g rat) reduced the blood pressure of SHR rats to 70% of the initial pressure; this pressure is almost the blood pressure of normal rats. Allopurinol (100  $\mu$ mol/300 g rat; i.v.) showed transient decrease in blood pressure and moderate reduction of **hypertension** of SHR (10%) was observed with i.v. injection of alloxanthine (100  $\mu$ mol/300 g rat). On the basis of these results, it seems that XO regulates EDRF/NO via production of O<sub>2</sub><sup>-</sup>.

L7 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:493848 CAPLUS  
DOCUMENT NUMBER: 125:184971  
TITLE: Allopurinol and glutamine attenuate bacterial translocation in chronic portal hypertensive and common bile duct-ligated growing rats  
AUTHOR(S): Schimpl, G.; Pesendorfer, P.; Steinwender, G.; Feierl, G.; Ratschek, M.; Hollwarth, M. E.  
CORPORATE SOURCE: Medical School, University Graz, Graz, A-8036, Austria  
SOURCE: Gut (1996), 39(1), 48-53  
CODEN: GUTTAK; ISSN: 0017-5749  
PUBLISHER: BMJ Publishing Group  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Spontaneous bacterial infections and septicemia result in morbidity and mortality in patients with portal **hypertension** and obstructive jaundice. The aim of this study in rats was to investigate the incidence of bacterial translocation in portal **hypertension** and obstructive jaundice, and to evaluate the effects of allopurinol and glutamine. Rats were subjected to sham laparotomy (SL), portal **hypertension** (PH) by calibrated stenosis of the portal vein, and common bile duct ligation (CBDL). Animals of each group were either treated with allopurinol (50 mg/kg twice a week), glutamine (1 g/kg/d), and allopurinol and glutamine. After four weeks, significant bacterial translocation in the untreated PH and CBDL rats occurred. Intestinal mucosal malondialdehyde concns. (MDA), as an indicator for lipid peroxidn., and myeloperoxidase activity (MPO) released from activated neutrophils were also significantly increased ( $p < 0.01$ ). Allopurinol and glutamine in PH and CBDL rats improved bacterial translocation, and decreased MDA and MPO values ( $p < 0.01$ ). In conclusion, in PH and CBDL rats significant bacterial translocation, ileal mucosal lipid peroxidn., and neutrophil derived MPO activity occurred. Allopurinol and glutamine significantly reduced bacterial translocation, as well as ileal mucosal MDA and MPO activities.

L7 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:664198 CAPLUS  
DOCUMENT NUMBER: 123:166783  
TITLE: Analysis of 135 cases of primary gouty arthritis  
AUTHOR(S): Yi, Wei; Liang, Xueping; Fan, Jiyuan; Zhang, Peng; Jia, Zhiheng  
CORPORATE SOURCE: Dep. Endocrinology, Tianjing Med. Univ., Tianjing, 300052, Peop. Rep. China  
SOURCE: Tianjin Yiyao (1995), 23(1), 3-6  
CODEN: TIYADG; ISSN: 0253-9896  
PUBLISHER: Tianjin Yixue Zazhishe  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB 135 Of primary gouty arthritis (134 males and 1 female) were complicated with obesity (51.7%), **hypertension** (43.7%) ischemia heart disease (25.2%), hyperlipemia (37.8%), nephrolithiasis (23.7%), s.c. trophic (18.5%), 15% of them had family history, onset age of gout

arthritis ranged from 21 to 74 yr (median 52 yr). After allopurinol therapy serum uric acid decreased from  $530.7 \pm 99.9 \mu\text{mol/L}$  ( $n = 135$ ) to  $240.9 \pm 66.6 \mu\text{mol/L}$  ( $n = 122$ ),  $p < 0.001$ , fractional clearance (CUA/Ccr) recovered from  $7.7 \pm 4.7\%$  ( $n = 96$ ) to  $19.4 \pm 12.6\%$  ( $n = 81$ ),  $p < 0.001$ . 87.6% Patients arthritis were relieved, the results suggested that the deficiency of renal uric acid clearance was involved in the pathogenesis of primary gout.

L7 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:309509 CAPLUS

DOCUMENT NUMBER: 122:71419

TITLE: Allopurinol fails to protect against gentamicin-induced renal damage in normotensive and spontaneously hypertensive rats

AUTHOR(S): Smyth, B.J.; Davis, W.G.

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC, 29425-2645, USA

SOURCE: Nephron (1994), 68(4), 468-72  
CODEN: NPRNAY; ISSN: 0028-2766

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent research suggests the involvement of hydroxyl and superoxide free radicals in the development of gentamicin-induced acute renal tubular necrosis. Xanthine oxidase has been implicated as an important source of superoxide free radicals. Spontaneously hypertensive (Wistar-Kyoto) rats (SHR) have excessive oxidant stress which may render them more sensitive to the reported oxygen free radical producing effects of gentamicin. This study was undertaken to determine if the xanthine oxidase inhibitor allopurinol will ameliorate the effects of gentamicin. Normotensive Wistar-Kyoto (WKY) rats and SHR were administered allopurinol (40 mg/kg twice daily) orally 4 days before and throughout a 12-day gentamicin treatment period. The allopurinol only treatment group demonstrated no noticeable histol. or functional changes considered to be indicative of nephrotoxicity. Gentamicin-injected WKY rats and SHR equally demonstrated extensive proximal tubular and glomerular damage characteristic of aminoglycoside-induced kidney damage. Allopurinol failed to protect either rat strain against the histol. damage caused by gentamicin. Equivalent alterations in serum creatinine, serum gentamicin, urinary N-acetyl- $\beta$ -D-glucos-aminidase excretion, body weight, urinary output, and blood pressure occurred in the gentamicin with allopurinol and gentamicin only treatment groups. Our results demonstrate allopurinol does not ameliorate the pathogenesis of gentamicin-induced renal damage. SHR do not appear to be more sensitive to the effects of gentamicin-induced kidney damage with or without allopurinol as compared with WKY rats.

L7 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:420255 CAPLUS

DOCUMENT NUMBER: 119:20255

TITLE: Protective effects of therapy with a protease and xanthine oxidase inhibitor in short form pancreatic biliary obstruction and ischemia in rats

AUTHOR(S): Hirano, Tetsuya; Manabe, Tadao; Steer, Michael; Printz, Hartmut; Calne, Roy; Tobe, Takayoshi

CORPORATE SOURCE: Dep. Surg., Addenbrookes Hosp., Cambridge, UK

SOURCE: Surgery, Gynecology and Obstetrics (1993), 176(4), 371-81  
CODEN: SGOBA9; ISSN: 0039-6087

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The current study was done to evaluate the effects of short term (60 min) pancreatic biliary duct obstruction (PBDO) with intraductal hypertension (IDH) stimulated by secretin (0.2 clin. unit per kg



per h) and caerulein (0.2 µg per kg per h) plus 30 min of temporary pancreatic ischemia (ISCH) produced by ligation of celiac and superior mesenteric artery on the exocrine pancreas and protective effects of a new potent protease inhibitor, ONO3307 in combination with xanthine oxidase inhibitor, allopurinol, in this multifactor related model of acute pancreatitis in rats. 12 H after PBDO with IDH plus ISCH, we observed hyperamylasemia; pancreatic edema into the pancreatic juice of rats stimulated by caerulein (control group-serum amylase levels,  $6 \pm 1$  units per mL; pancreatic water content,  $74 \pm 1$  percent. Furthermore, PBDO with IDH plus ISCH caused the redistribution of lysosomal enzyme from lysosomal fraction to zymogen fraction. Only PBDO with IDH caused no significant changes. Although only ONO3307 or allopurinol therapy showed the partial significant protective effects against pancreatic injuries, improving serum amylase levels, the administration of ONO3307 in combination therapy with allopurinol showed almost complete protective effects against the pancreatic injuries induced by PBDO with IDH plus ISCH (serum amylase levels,  $9 \pm 2$  units per mL; pancreatic water content,  $76 \pm 2$  percent; amylase and cathepsin B output,  $7,127 \pm 946$  and  $18 \pm 3$  units per kg per h; 1.3 kilo times gravity pellet,  $28 \pm 2$  percent; 12 kilo times gravity pellet,  $54 \pm 2$  percent, and energy charge equals  $0.85 \pm 0.02$ ). These results indicate the important roles of temporary pancreatic ischemia and oxygen derived free radicals in the pathogenesis of pancreatic damages in this PBDO with IDH plus ISCH reperfusion in the rat model and the usefulness of combination therapy of such a new potent protease inhibitor and xanthine oxidase inhibitor, such as allopurinol, in the treatment of clin. acute pancreatitis.

L7 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:199354 CAPLUS

DOCUMENT NUMBER: 114:199354

TITLE: Nephrotoxicity of allopurinol is enhanced in experimental **hypertension**

AUTHOR(S): Trachtman, Howard; Valderrama, Elsa; Futterweit, Stephen

CORPORATE SOURCE: Dep. Pediatr., Schneider Child. Hosp., New Hyde Park, NY, 11042, USA

SOURCE: Hypertension (1991), 17(2), 194-202  
CODEN: HPRTDN; ISSN: 0194-911X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hyperuricemia is present in 20-40% of pediatric and adult patients with essential **hypertension**. This metabolic abnormality may represent an addnl. risk factor for the development of cardiovascular disease. Therefore, the authors performed the following studies to determine 1) whether hyperuricemia is more prevalent in the spontaneously hypertensive rat (SHR) and 2) whether allopurinol treatment has a beneficial effect on the development of **hypertension** in this strain, based on its capacity to lower the serum uric acid concentration and to act as an antioxidant agent. SHR and control Wistar-Kyoto (WKY) rats were assigned to two groups, one given tap water to drink and the other provided water containing allopurinol (400 mg/L) to furnish an approx. daily dose equal to 100 mg/kg. This treatment was maintained for 15 wk. The serum uric acid levels were similar in untreated SHR and WKY rats (1.85 vs. 1.66 mg/dL). In the control WKY rat strain, allopurinol therapy did not adversely affect weight gain or hematocrit and did not cause an increase in mortality. It resulted in a moderate decrement in kidney function (creatinine clearance: allopurinol-treated group 0.32 vs. control group 0.46 mL/min/100 g body wt, in conjunction with mild-to-moderate tubulointerstitial inflammation (allopurinol-treated group 0.9 vs. control group 0). In contrast, administration of allopurinol to SHR resulted in failure to thrive, marked anemia, severe azotemia (creatinine clearance: allopurinol-treated group 0.04 vs. control group 0.39 mL/min/100 g body weight;  $p < 0.001$ ), and severe tubular atrophy and interstitial fibrosis (allopurinol-treated group 2.2 vs. control group 0). These findings

indicate that hyperuricemia is not more prevalent in the SHR. Furthermore, allopurinol administration is associated with markedly increased nephrotoxicity characterized by severe tubulointerstitial injury, azotemia, and impaired growth.

L7 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:69302 CAPLUS  
DOCUMENT NUMBER: 110:69302  
TITLE: The malonyldialdehyde levels in the cerebral tissue after reperfusion following the occlusion of the bilateral common carotid artery in spontaneously hypertensive rats and the effect of allopurinol, a xanthine oxidase inhibitor  
AUTHOR(S): Kawakami, Masato; Itoh, Toru; Tochigi, Shoichiro  
CORPORATE SOURCE: Sch. Med., St. Marianna Univ., Japan  
SOURCE: Nosotchu (1988), 10(5), 400-3  
CODEN: NOSOD4; ISSN: 0912-0726  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese

AB Using spontaneously hypertensive rats, the authors studied the effect of allopurinol, a xanthine oxidase inhibitor, on lipid peroxidn. in the cerebral tissue after reperfusion for 30 min following the occlusion of the bilateral common carotid artery for 3 h. In the present study, the malonyldialdehyde (MDA) values were measured as indicators for lipid peroxides in the cerebral tissue, and compared them between the group pretreated with oral administrations of allopurinol (400 mg/kg) and the nontreated control group. As a result, the MDA value measured were found to be 68.9 nmol/gm in the Sham-operated group and 83.27 nmol/gm in the control group. However, the allopurinol-treated group showed a level as low as 67.62 nmol/gm which was significant compared to that of the control group. These results suggest the possibility that allopurinol inhibits the lipid peroxidn. caused by the xanthine oxidase-linked free radical induced by cerebral ischemia and reperfusion.

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ACCESSION NUMBER: 1969:429245 CAPLUS  
DOCUMENT NUMBER: 71:29245  
TITLE: Hyperlipemia following allopurinol administration  
AUTHOR(S): Thibodeau, G. A.; Felker, J. R.; Swanson, R. N.  
CORPORATE SOURCE: South Dakota State Univ., Brookings, SD, USA  
SOURCE: South Dakota Journal of Medicine (1969), 22(4), 40-2  
CODEN: SDMEAL; ISSN: 0038-3317  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Allopurinol (I) in a single clin. case and in a preliminary animal study caused hyperlipemia. A male patient diagnosed as having primary gout and benign essential **hypertension** was placed on allopurinol therapy (100 mg. 4 times/day together with colchicine at 0.65 mg./day). Marked increase in serum lactescence was noted after initiation of therapy. Blood anal. made 2 months after initiation of therapy showed total lipids 4287, phospholipids 876, and triglycerides 2245 mg. %. Allopurinol therapy was discontinued. Blood anal. made 2 weeks later showed total lipids 2640 phospholipids 396, and triglycerides 1100 mg. %. Rabbits were given I (50 mg./day) for 2 weeks. Blood samples obtained by cardiac puncture were then tested for pre- and posttreatment total serum cholesterol levels. A 17.5% increase in total serum cholesterol was found.

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ACCESSION NUMBER: 1967:452640 CAPLUS  
DOCUMENT NUMBER: 67:52640  
TITLE: Allopurinol in thiazide-induced hyperuricemia  
AUTHOR(S): Rapado Errazti, Aurelio

CORPORATE SOURCE: Fundacion Jimenez-Diaz, Madrid, Spain  
SOURCE: Annals of the Rheumatic Diseases, Supplement (1966), 6, 660-7  
CODEN: ARHSB7  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Allopurinol (I) given to normal subjects decreased serum and urinary uric acid (II) levels. There was no significant change in urate clearance (Curate) or in the ratio of urate-to-creatinine clearance (Ccreatinine). I and thiazide diuretics given together caused serum II to increase and Curate to decrease with no effect on urinary II. The effect of I alone on hypertensive patients with normal kidney function was the same as for controls. The diuretic increased serum II, and decreased Curate and the Curate-to-Ccreatinine ratio. Diuretics given during I treatment had no effect on serum or urinary II. Thiazide decreased the glomerular filtration rate (GFR) and the ratio of Curate-to-Ccreatinine. Gouty hypertensive patients with normal renal function previously treated with I did not have significantly increased serum II nor decreased Curate levels after thiazide administration. The GFR decreased in gouty hypertensive patients with impaired renal function. There was no hyperuricemic response nor variation in Curate. The ratio of Curate-to-Ccreatinine increased. After I administration, serum and urinary II returned to normal in hypertensives with thiazideinduced hyperuricemia. Gouty hypertensives previously treated with thiazides had normal serum II and decreased urinary II after I administration. These patients previously treated with I had no significant differences in serum or urinary II after diuretic administration. I had no effect on the hypotensive action from diuretic administration. In some gouty patients where serum II was restored to normal by I, thiazide precipitated an acute attack mainly at the beginning of treatment. The serum II level was appreciably less than before treatment. Increased doses of colchicine controlled the attack. There were no alterations in blood pressure or hepatic function during I administration.